

**439 CF Registries – plea for annual reports focusing on patients homozygous for the F508del mutation**

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**Background:** Beyond the need for harmonizing definitions, a number of factors can impact on and/or hamper comparisons between registries and even within registries over time (exhaustivity rate, genetic background, availability of specialized diagnostic tools, CF NBS, quality of care ...).

**Aim:** Using data from the Belgian CF Registry over a 10-y period (2007: n = 1.047, 1998: n = 564), we aimed to compare important characteristics of registered patients.

**Results:** There were significant increases in the proportions of adults (38.8 to 49.3%,  $p < 0.0001$ ), patients diagnosed  $>18$  y (4.2 to 7.7%,  $p = 0.003$ ), PS patients (6.2 to 12.9%,  $p < 0.0001$ ), patients with intermediate sweat chloride values (30–60 mmol/L) (1.2 to 9.1%,  $p < 0.0001$ ). The percentage of patients homozygous for the F508del mutation (F508delH) decreased (54.9 to 46.9%,  $p = 0.001$ ). In 2007, 51.7% of non-transplanted children (6– $<18$  y) had a FEV1  $\geq 90\%$  pred (Knudson) vs 32.3% in 1998 ( $p < 0.0001$ ) but this improvement was more marked for PS patients (33.3 to 75%) than for F508delH (32.2 to 43.4%).

**Conclusion:** Deriving from each national annual report a parallel report focusing on patients homozygous for the F508del mutation would limit some pitfalls encountered when trying to compare data from different countries and allow more meaningful longitudinal analysis of outcomes in a given country. Additional costs would be negligible.

**440 UMD-CFTR-France: a model of national database for collection and analysis of extensive molecular data in CF and CFTR-related diseases (CFTR-RD)**

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CF and particularly CFTR-RD provide a challenge for molecular diagnostic because of many unclassified variants (UV) and identical genotypes associated with different phenotypes. There is a need for an accurate and exhaustive collection of sequence variations identified in patients suffering from disease related with the CFTR gene as most of these variants reside in genetic testing laboratories and remain unpublished. Since 2009, we have collected and curated molecular and minimal clinical data from 9 French expert laboratories. Using the Universal Mutation Database (UMD<sup>®</sup>) software, we have constructed the UMD-CFTR-France, an exhaustive and manually-curated database, dedicated to sequence variations of the CFTR gene identified in CF and CBAVD patients, in patients analysed in the context of newborn screening, chronic rhinosinusitis, bronchiectasis, pancreatitis, nasal polyposis, fetal bowel anomalies, and compound heterozygous unaffected parents.

This database currently contains molecular data on 2426 patients: 1837 CF and 589 CFTR-RD mostly represented by CBAVD (490). Besides disease-causing mutations, it contains UVs and non-pathogenic polymorphisms (532 different variants) representing 7488 entries.

Pooling of these data could significantly advance the interpretation of rare variants and the analysis of correlations between genotype/haplotype and phenotype. The strength of this interpretation and analysis is based on the large number of high quality data and dedicated bioinformatics tools.

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**441 CF quality assurance in Germany: MUKO.dok as a specific database developed for analysis and out-patient clinic management**

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The German CF quality assurance project was established in 1995. The overall aim is to improve quality of life and survival in CF patients. Data collection is an essential tool in this quality management process. From the beginning data collection was achieved electronically. Since 2008 a new specific database is under development. Aim of this work is to create a software allowing not only the collection of patient data but also the management of medical and administrative process in the outpatient clinic. Information on routine clinical and lab data, bacteriology, therapy and specific outcomes on local and national level are available. The system is implemented in a client-server-application. The server allocates the central database (Oracle). The software should optimize performance of storage, search and analyzing data on patients with CF. In 2008 7,644 patients have been treated in 93 centres. The annual return was improved to 84%. Demographic, nutritional and lung function data are given and specified for the centres. Mortality analysis and longitudinal data are included. Comparison of patient data between different centres and national registry has been done. The data is also provided anonymously to the ECFS registry.

**442 Cystic fibrosis in Republic of Moldova**

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**Actuality:** 57 patients with cystic fibrosis (CF) are evaluated and treated in Clinic of Pneumology, Republic of Moldova.

**Aim:** In this work we assessed the peculiarities of genetic findings, clinical symptoms and explorative picture in children with CF from Republic of Moldova.

**Materials and Methods:** This study included 29 boys, 28 girls, mean age  $8.91 \pm 0.45$  years. Genetic diagnosis was realized in children and their parents for 4–8 CFTR mutations (F508del, R334W, N1303, G551D, R347P, R553X, R117H, W1282X, G542X). More rare mutations were revealed in Center of Bordeaux. The evaluation program for CF patients include: anthropometry, chest radiography, computed tomography (CT), spirometry, sputum bacteriology, serum biochemistry, coprology.

**Results:** F508del mutation was revealed in 57.8% cases (inclusive 24.5% – homozygotes), 1 child – N1303K, 1 case – R334W. In Bordeaux were discovered mutation in 4 children (F508del/296+1G>C, F508del/185+1G>T, G542X/N1303K, 128+1G>A/1677delTA). The mean age of CF diagnosis was  $2.65 \pm 0.05$  years: at the age of  $<1$  year in 52.6% children, 1–5 year – 38.5% children, 5–10 years – 7.1% cases, 10–18 years – 8.7% children, 19 years – 1.7% cases. *Ps. aeruginosa* was isolated in 47.3% cases. CT has revealed bronchiectasis (34.3% cases), pulmonary fibrosis (23.8% cases) and chronic bronchitis (68.8% cases). Spirometry showed pulmonary function impairments (FVC –  $65.8 \pm 2.2\%$ , FEV1 –  $68.8 \pm 2.6\%$ ). Nutrition impairment was established in 71.5% CF patients.

**Conclusion:** Lung affecting and nutrition problems are present in most children with CF from Moldova. There is a prevalence F508del CFTR mutation in CF patients in Moldova.